METHOD FOR THE PREDICTION OF BINDING TARGETS AND THE DESIGN OF LIGANDS

ABSTRACT

A computer-based method for the identification of binding targets in proteins and other macromolecules. More particularly, the invention includes an algorithm aimed at predicting binding targets in proteins. This algorithm, named Woolford, requires knowledge of the high resolution structure of the protein but no knowledge of the location or identity of natural binding sites or ligands. Binding targets in the protein are identified and classified according to their expected optimal affinities. Binding targets can be located at the protein surface or at internal surfaces that become exposed as a result of partial unfolding, conformational changes, subunit dissociation, or other events. The entire protein is mapped according to the binding potential of its constituent atoms. Once binding targets are identified, optimal ligands are designed and progressively built by the addition of individual atoms that complement structurally and energetically the selected target. This algorithm is expected to have significant applications in structure-based drug design since it allows: 1) identification of binding targets in proteins; 2) identification of additional targets if the primary target is known; 3) design of ligand molecules with optimal binding affinities for the selected target; and 4) refinement of lead compounds by defining the location and nature of chemical groups for optimal binding affinity.

309981.B11